

Thermodynamic properties of inclusion complexes of α -cyclodextrin + aliphatic nitriles ($\text{H}(\text{CH}_2)_n\text{CN}$; $n = 1\text{--}8$) in aqueous solution

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Abstract In order to investigate the contribution of the hydrophilic parts of guest molecules of aliphatic complexes to the inclusion reaction, the thermodynamic properties of inclusion complexes of cyclodextrin (α -CD) with aliphatic nitriles [$\text{H}(\text{CH}_2)_n\text{CN}$; $n = 1\text{--}8$] into the α -CD cavity in dilute aqueous solutions were measured by a micro-calorimeter at 298.15 K. The thermodynamic properties of inclusion for the octane nitrile system were different from those of others. The inclusion process of aliphatic nitriles to α -CD has two kinds of major driving force of enthalpy and entropy driven inclusion. The interaction energies of inclusion complexes of α -CD and aliphatic nitriles were determined by DFT calculation (B3LYP/6-31++G (d,p)) in water and compared with the experimental results. DFT calculations were performed on the inclusion complexes of α -CD with seven nitriles of each conformer. Both the gas phase interaction and solvent effect were taken into consideration. Also non-polar interactions between aliphatic nitriles + α -CD in aqueous solution were calculated and herein the inclusion energy is discussed.

Keywords Thermodynamic properties · Molecular inclusion · Aliphatic nitriles α -cyclodextrin · Aqueous solutions · DFT

Introduction

Cyclodextrin (CD) molecules include many kinds of guest molecules in their molecular cavities reflecting the differences in structure with those in aqueous solutions. In order to investigate the contribution of the size of the hydrophobic parts and the positional effect of polar groups of a guest molecule on inclusion reactions, the thermodynamic properties of inclusion complexes of CD with aliphatic alcohols and other alcohols have been investigated systematically by the author's group [1–12] and others [13–23]. The thermodynamic properties of aliphatic alcohols show similar behaviors [7]. Enthalpies and entropies of inclusion were increased with increasing the size of aliphatic groups until pentanol. The Gibbs energies of inclusion pentane derivatives were larger than those in each homological system [7]. The inclusion process may separate two kinds of opposite and/or cooperative effects from guest molecules. One is from aliphatic groups of the non-polar effect and the other is a functional group of polar groups usually. In order to elucidate the polar group effect of guest molecules on the inclusion properties, pentane derivatives of nitrile, amine, nitro, thiol, fluoride, chloride, bromide, iodide and carboxylic acid, thermodynamic properties of pentane derivatives have been determined [7]. In this article, in order to clarify the basic problems of size of the non-polar group and polar group of guest molecules systematically, the molar enthalpies, entropies and Gibbs energies of inclusion of seven aliphatic nitriles into α -CD cavities at 298.15 K in dilute aqueous solutions were determined at 298.15 K, and compared with those of aliphatic alcohols.

Also, to elucidate the interaction energies of non-polar group effect on inclusion for α -CD and aliphatic nitriles in the gas phase and aqueous solution, DFT calculations were performed.

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Experimental

Materials

Aliphatic nitriles ($\text{H}(\text{CH}_2)_n\text{CN}$; $n = 1-8$) (Tokyo Kasei Co.) were fractionally distilled over freshly activated 4A molecular sieves that had been evacuated at 453 K for 12 h under 10^{-2} – 10^{-3} Pa. Their chemical purities, obtained from gas chromatography by each using a 2 m column of 10% SE-30 on chromosorb and 20% PEG-1000 on Celite 545 with FID on a Yanagimoto G180FP, were more than 99.9%. Water contents were obtained by a Coulometric Karl-Fischer method on a Moisturemeter (Mitsubishi Chemical Ind., CA-02) at less than 0.01 mol%. $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$, 18-crown-6 (1,4,7,10,13,26-hexaoxacyclooctadecane, Kishida Chemical Co.) were recrystallized. The purity and water content were determined by TG-DTA and DSC (TG8101D, DSC8240, Rigaku Co.) [24], and more than 99.9%.

Details of the careful purification used for the α -CD [1] and water [25] have been described previously. All aqueous solutions were prepared by mass to maintain five significant figures. Especially higher aliphatic nitriles were not highly soluble in water. So aliphatic nitriles were weighed at 30–600 mg by a microbalance (Mettler ME30, 1- μg precision) in a glass vial. Water was weighed by a 1 kg balance (Murakami 10-mg precision) in a well sealed vessel. The glass vial containing aliphatic nitriles was crushed in a vessel containing ca., 1 kg water. The aqueous solutions prepared were stirred for 30 min at room temperature with a magnetic stirrer. Then, they were stirred vigorously for ca. 15 min at room temperature with a supersonic washer (Taga Electric Co., Ltd., model UW-25, output frequency: 38 kHz, 45 W).

Apparatus

A twin-microcalorimeter of the heat-conduction type, Thermal Activity Monitor (Thermometric AB, Järfälla, Sweden) with 3 cm³ volume of mixing vessels, which we previously modified [26, 27], was used for measuring the excess enthalpies at 298.15 K. A reliability test of the microcalorimeter system and the procedures used had been performed using binary mixtures of (1 - x)1,4-dimethylbenzene + x 1,3-dimethylbenzene and (1 - x)1,4-dimethylbenzene + x 1,2-dimethylbenzene as reported previously [26] for exothermic and endothermic systems. The precision was more than 0.1% for enthalpies of mixing compared with three difference principle calorimeters and references. And to confirm the results of the titration experiments, the binding thermodynamic properties were determined following the IUPAC recommendations [28]. The binding constant and enthalpies of Ba^{2+} and 18-crown-6 were (5905 ± 8) mol dm⁻³, $-(31.44 \pm 0.15)$ kJ mol⁻¹, respectively, which agreed with the recommended values in experimental error.

Determination of interaction energy

The initial structure of α -CD was obtained from the crystal structure [29]. Nitriles were optimized with MP2/6-311++G** in the gas phase and solvent of water by the self-consistent reaction field (SCRF) calculation [30, 31]. And the inclusion complexes of α -CD and aliphatic nitriles were optimized with B3LYP/6-31++G(d,p) in the gas phase and solvent of water by the SCRF calculation. All the calculations were performed with GAUSSIAN 09 [32]. Interaction energies and thermodynamic properties were calculated by the supermolecular method [31]:

Results and discussion

Enthalpy of dilution

The experimental results of the enthalpy changes on diluting the dilute aqueous aliphatic nitriles solutions ranging from 0.8×10^{-5} to 4.9×10^{-5} in mole fraction at 298.15 K under atmospheric pressure are given in Table 1, where n_3 denotes the amount of aliphatic nitriles in the solutions and x_i and x_f , respectively, are the mole fractions before and after the dilution.

The results were fitted to Eq. 1 by the least-squares calculation [33].

$$\Delta_{\text{dil}}H = an_3(x_i - x_f) + bn_3(x_i^2 - x_f^2) + \dots \quad (1)$$

The best-fit values for the parameters in Eq. 1 are listed in Table 2, as well as the standard deviation of the fit s_f . However, the enthalpy changes on diluting the dilute aqueous octane nitrile were negligibly small and within experimental error in this concentration range. So those changes were excluded from the following calculation.

Enthalpy of transfer

The thermochemical cycle for the enthalpy of transfer is shown in Fig. 1. The experimental enthalpies of transfer of aliphatic nitriles from dilute aqueous solutions to dilute aqueous α -CD solutions determined by Eq. 2 [7, 8] are also summarized in the last column of Table 3.

$$\Delta_{\text{trf}}H = \Delta_{\text{mix}}H - \Delta_{\text{dil}}H_{12} - \Delta_{\text{dil}}H_{13} \quad (2)$$

Here 1, 2, 3, 12, and 13 showed water, α -CD, aliphatic nitriles, aqueous solution of α -CD and aqueous solution of aliphatic nitriles, respectively. The experimental results for the enthalpy changes of α -CD solution [8], $\Delta_{\text{dil}}H_{12}$, were obtained from our earlier papers [8]. In the calculation through Eq. 2, the enthalpies of dilution of aqueous aliphatic nitriles solution, $\Delta_{\text{dil}}H_{13}$, were determined by

Table 1 Experimental enthalpies of dilution $\Delta_{dil}H$ of R-CN in the aqueous solution with water at 298.15 K

$10^5 n_3/\text{mol}$	$10^5 x_i$	$10^5 x_f$	$\Delta_{dil}H_m/\text{mJ}$
H₂O + ethylnitrile			
0.7341	4.894	4.840	0.111
0.7341	4.840	4.788	0.071
0.7341	4.788	4.736	0.062
0.7341	4.736	4.686	0.091
0.7341	4.686	4.637	0.083
0.7341	4.637	4.588	0.091
0.7341	4.588	4.541	0.079
0.7341	4.541	4.495	0.094
0.7341	4.495	4.449	0.058
0.7341	4.449	4.405	0.079
H₂O + propylnitrile			
0.7285	4.856	4.803	0.132
0.7285	4.803	4.751	0.082
0.7285	4.751	4.700	0.081
0.7285	4.700	4.650	0.098
0.7285	4.650	4.601	0.085
0.7285	4.601	4.553	0.097
0.7285	4.553	4.506	0.119
0.7285	4.506	4.460	0.123
0.7285	4.460	4.415	0.061
0.7285	4.415	4.371	0.087
H₂O + butylnitrile			
0.7122	4.748	4.696	0.129
0.7122	4.696	4.645	0.085
0.7122	4.645	4.595	0.070
0.7122	4.595	4.546	0.091
0.7122	4.546	4.498	0.084
0.7122	4.498	4.451	0.093
0.7122	4.451	4.405	0.088
0.7122	4.405	4.361	0.104
0.7122	4.361	4.316	0.069
0.7122	4.316	4.273	0.073
H₂O + pentanenitrile			
0.6758	4.748	4.696	0.141
0.6758	4.696	4.645	0.116
0.6758	4.645	4.595	0.113
0.6758	4.595	4.546	0.083
0.6758	4.546	4.498	0.071
0.6758	4.498	4.451	0.062
0.6758	4.451	4.405	0.117
0.6758	4.405	4.361	0.122
0.6758	4.361	4.316	0.054
0.6758	4.316	4.273	0.068
H₂O + Hexanenitrile			
0.2706	1.804	1.784	-0.020
0.2706	1.784	1.765	-0.029

Table 1 continued

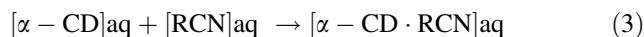
$10^5 n_3/\text{mol}$	$10^5 x_i$	$10^5 x_f$	$\Delta_{dil}H_m/\text{mJ}$
0.2706	1.765	1.746	-0.014
0.2706	1.746	1.727	-0.018
0.2706	1.727	1.709	-0.023
0.2706	1.709	1.691	-0.031
0.2706	1.691	1.674	-0.055
0.2706	1.674	1.657	-0.025
0.2706	1.657	1.640	-0.024
0.2706	1.640	1.623	-0.018
H₂O + heptanenitrile			
0.1354	0.9029	0.8930	-0.056
0.1354	0.8930	0.8833	-0.040
0.1354	0.8833	0.8738	-0.028
0.1354	0.8738	0.8645	-0.012
0.1354	0.8645	0.8554	-0.027
0.1354	0.8554	0.8465	-0.003
0.1354	0.8465	0.8377	-0.027
0.1354	0.8377	0.8292	-0.035
0.1354	0.8292	0.8208	-0.011
0.1354	0.8208	0.8126	-0.018

Table 2 Best fits coefficients of a and b in Eq. 1 and the standard deviations of the fit s_f

	$10^9 a/\text{J mol}^{-1}$	$10^9 a^e/\text{J mol}^{-1}$	$10^{14} b/\text{J mol}^{-1}$	$10^{14} b^e/\text{J mol}^{-1}$	s_f/mJ
Ethylnitrile	28.04	0.047	-0.5669	0.51	0.016
Propylnitrile	38.00	0.068	-1.159	0.73	0.023
Butylnitrile	1.632	0.052	2.719	0.58	0.017
Pentylnitrile	-87.56	0.085	12.98	0.94	0.026
Hexanenitrile	-324.9	0.257	79.38	7.5	0.012
Heptanenitrile	1854	1.1	-120.4	65.0	0.013

a^e, b^e showed estimation error

Eq. 1 with the parameters given in Table 2. For the equilibrium of a 1:1 complex formation given in Eq. 3 [7]



Equilibrium constant K is shown as Eq. 4

$$K = \frac{\frac{n_4}{n_1+n_2+n_3-n_4}}{\frac{n_2-n_4}{n_1+n_2+n_3-n_4} \cdot \frac{n_3-n_4}{n_1+n_2+n_3-n_4}} \quad (4)$$

where $n_1, n_2, n_3,$ and n_4 mean, respectively, the amounts of water, α -CD, aliphatic nitriles and 1:1 complex in the aqueous solution. The molar ratio y of aliphatic nitriles included in the cavities over the total aliphatic nitriles in the solution is given by Eq. 6:

$$y = n_4/n_2, \quad w = n_2/n_3, \quad z = n_1/n_3 \quad (5)$$

$$y = \frac{1}{2} + \frac{1}{2w} + \frac{z}{2w(1+K)} - \sqrt{\left(\frac{1}{2} + \frac{1}{2w} + \frac{z}{2w(1+K)}\right)^2 - \frac{K}{w(1+K)}} \quad (6)$$

Equation 6 can be written as follows:

$$(w + Kw)y^2 - (1 + w + z + Kw + K)y + K = 0 \quad (7)$$

Here $0 \leq y \leq 1$

$$\Delta_{\text{trf}}H_m^\infty = \Delta_{\text{trf}}H_m \cdot \frac{y_{\text{max}}}{y} \quad (8)$$

Since the molar enthalpy of the transfer of aliphatic nitriles is proportional to y , the experimental function and the theoretical one are equivalent as shown in Eq. 9:

$$\Delta_{\text{inc}}H_m = \frac{\Delta_{\text{trf}}H_m^\infty}{y_{\text{max}}} \quad (9)$$

Here y_{max} , limiting ratios of aliphatic nitriles included excess total aliphatic nitriles in the systems at infinite dilution. By the least-squares treatment of the experimental values of $\Delta_{\text{trf}}H_m$ as a function of z and the pseudo binary mixture's mole fraction of aliphatic nitriles, $f = n_3/(n_2 + n_3)$, according to Eq. 10 described in an earlier paper of this series [7], limiting molar enthalpies of transfer at infinite dilution, $\Delta_{\text{trf}}H_m$, were determined as well as the equilibrium constants K of 1:1 inclusion complexes formation and y_{max} . The values of $z = n'_1 + n''_1/n_2$ [7, 8] depended on the solubility of aliphatic nitriles. Here n'_1 and n''_1 showed the amounts of water before and after mixing in mol, respectively, as shown in Fig. 1. The z of systems of hexane nitrile, heptane nitrile, and octane nitrile are the solubility problem. These quantities thus determined are summarized in Table 3. The smoothed values of $\Delta_{\text{trf}}H_m$ for mean values of z are drawn in Fig. 2 against the mole fraction f . The molar enthalpies of transfer of aliphatic nitriles were negative values for the α -CD solutions as shown in Fig. 2. Enthalpies of transfer of aliphatic nitriles were decreased with increasing the aliphatic chain until pentane nitrile. And the sequence of stabilization of

enthalpy of transfer at $f = 0.2$: octane nitrile > butane nitrile > heptane nitrile > hexane nitrile > propane nitrile > ethane nitrile > methane nitrile. The enthalpies of transfer of aliphatic nitriles in the α -CD might have the same size effect of interaction between the inner cavity of α -CD and aliphatic groups of nitriles as with the aliphatic alcohols as reported previously [7].

Table 3 Equilibrium constants for the formation of 1:1 inclusion ratios of water molecules over α -CD, limiting molar enthalpies of transfer of α -CD + aliphatic nitrile and the limiting molar ratios y'_{max} of α -CD including at 298.15 K

	log K	z_0	$\Delta_{\text{trf}}H_m^\infty/\text{J mol}^{-1}$	y'_{max}
Ethyl nitrile	4.1	21563	-0.61	0.378
Propyl nitrile	3.8	22222	-1.64	0.218
Butyl nitrile	4.3	21061	-3.57	0.487
Pentyl nitrile	10.6	21013	-7.25	0.651
Hexanenitrile	10.1	55556	-6.19	0.270
Heptanenitrile	0.26	111753	-6.92	0.263
Octanenitrile	5.58	214500	-8.15	0.639

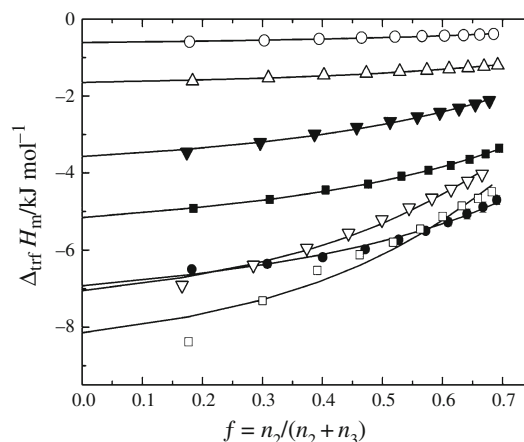
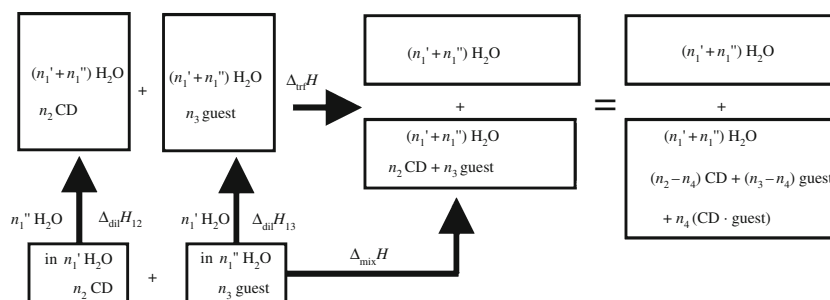


Fig. 2 Molar enthalpies of transfer of aliphatic nitriles ($\text{H}(\text{CH}_2)_n\text{CN}$; $n = 1-8$) from aqueous to aqueous α -CD solutions at 298.15 K as a function of $f = n_2/(n_2 + n_3)$: $n = 1$, open circle, $n = 2$; open triangle, $n = 3$; filled upside triangle, $n = 4$; open filled upside triangle, $n = 5$; filled square, $n = 6$; filled circle, $n = 7$; open square $n = 8$

Fig. 1 Thermochemical cycle for determining the enthalpies of transfer: n_1, n_2, n_3 , and n_4 show the amounts of water, α -CD, aliphatic nitriles and 1:1 complex in the aqueous solution, respectively



Enthalpy and entropy of inclusion

From the thermodynamic functions listed in Table 3, the molar enthalpies, molar Gibbs energies and molar entropies of inclusion of aliphatic nitriles at infinite dilution into α -CD cavities in aqueous solutions at 298.15 K were determined and are summarized in Table 4. The enthalpies of inclusion of all aliphatic nitriles with α -CD are exothermic from -1.2 to -26.3 kJ mol $^{-1}$ and stabilized on inclusion with guest molecules. The enthalpies of inclusion of hexane nitrile acid and ethane nitrile showed the largest and least enthalpic stabilization, respectively. Molar Gibbs energies of inclusion of α -CD + nitriles are also plotted in Fig. 3 with reported values of α -CD + aliphatic alcohols [3]. All molar Gibbs energies of inclusion of α -CD + nitriles were negative and stabilized at more than -22 kJ mol $^{-1}$ on inclusion. The Gibbs energies of inclusion of octane nitrile and propane nitrile showed the largest and least enthalpic stabilization, respectively. The sequence of Gibbs energetic stabilization in aliphatic nitriles was not simple as with the aliphatic alcohols [7] as shown in Fig. 3.

Enthalpic stabilization of inclusion for α -CD + aliphatic nitriles was increased with increasing the methylene groups in aliphatic nitriles except octane nitrile as shown in Fig. 4. And entropies of inclusion of aliphatic nitriles + α -CD measured were positive except those of heptane nitrile. Entropic stabilization of inclusion for α -CD + aliphatic nitriles was decreased with increasing the methylene groups in aliphatic nitriles except heptane nitrile. From a thermodynamic perspective, there are two kinds of inclusion mechanism as shown in Fig. 4. One is entropy driven inclusion such as the processes of ethane, propane, butane, and pentane nitrile. However, the inclusion processes of heptane nitrile and octane nitrile were different from the others. Their mechanism of enthalpy driven inclusion is shown in Fig. 4.

Table 4 The changes of thermodynamic properties of 1:1 inclusion compounds of α -CD + guest nitrile molecule in aqueous solutions at 298.15 K

Guest	$\Delta_{\text{inc}}G/\text{kJ mol}^{-1}$	$\Delta_{\text{inc}}H/\text{kJ mol}^{-1}$	$T\Delta_{\text{inc}}S/\text{kJ mol}^{-1}$	$\Delta_{\text{inc}}S/J(\text{K mol}^{-1})$
Ethyl nitrile	-23.4	-1.19	22.2	74.5
Propyl nitrile	-21.6	-7.52	14.1	47.4
Butyl nitrile	-24.6	-7.33	17.2	57.8
Pentyl nitrile	-26.2	-11.13	15.1	50.6
Hexanenitrile	-24.6	-22.92	1.7	5.7
Heptanenitrile	-26.3	-26.31	0.0	-0.2
Octanenitrile	-31.8	-12.75	19.1	64.0

Stability of guest molecules in the α -CD cavity

Stabilization on inclusion between α -CD + aliphatic nitriles might not be a small effect on van der Waals interaction between the hydrophobic part of aliphatic nitriles and the hydrophobic inner wall of α -CD. Then the contact surface area between aliphatic nitriles and the inner wall of α -CD might make a large contribution toward stabilization of inclusion.

Aliphatic nitriles have conformers for *trans*, *cis*, and *gauche* from pentane nitrile to octane nitrile. There are 21,840 conformers from acetonitrile to octane nitrile. However, aliphatic nitriles used from butane nitriles to octane nitrile can have 340 conformers by steric hindrance of atomic orbitals. These conformers were optimized in the gas phase by MP2/6-311++G** with GAUSSIAN 09 [31]. In order to find the bulkiest conformer of each nitrile, the distance between the head to tail of nitriles was determined

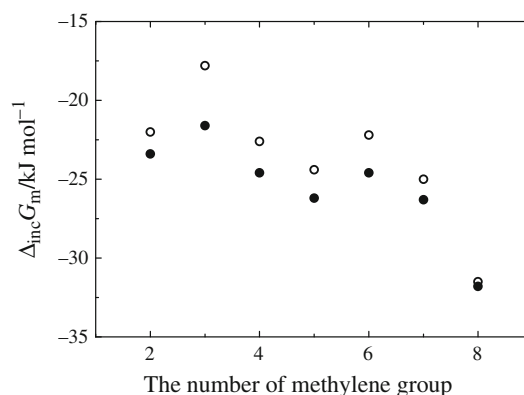


Fig. 3 The change of Gibbs energies of inclusion α -CD + Guest molecules at 298.15 K against the number of alkyl chains: filled circle aliphatic nitriles; open circle aliphatic alcohols [7]

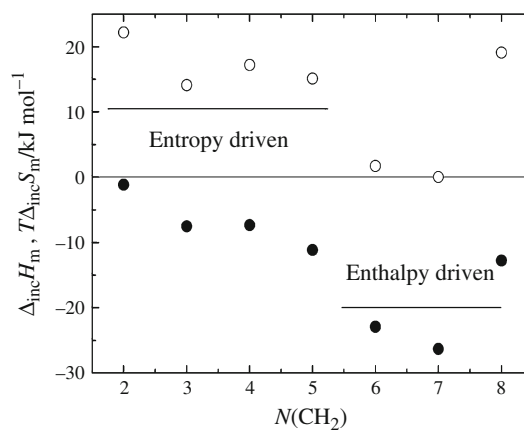


Fig. 4 The changes of enthalpies and entropies of inclusion α -CD + nitriles at 298.15 K against the number of methylene groups: filled circle $\Delta_{\text{inc}}H$ enthalpy changes of inclusion, open circle $T\Delta_{\text{inc}}S$ entropy changes of inclusion

for each nitrile. And the nitriles with the longest distance of head to tail were all *trans* formed nitriles. Other conformers are summarized in the second column in Table 5.

All the calculations were performed with GAUSSIAN 09. α -CD from the crystal structure [29] and aliphatic nitriles were optimized with B3LYP/6-31G(d,p) in solvent of water by SCRF calculation [30]. The inclusion complex of α -CD and the aliphatic nitriles were constructed from the B3LYP/6-31++G(d,p)- optimized CD and the aliphatic nitriles. The position of the substrate was defined by its Z coordinate. The inclusion complexes were emulated by entering the guest molecules from the secondary hydroxyl side of the CD with both sides of the guest molecules. The geometry of the complex was completely optimized with B3LYP/6-31++G(d,p) without any restriction in the gas phase and in water solution by using the Onsager continuum solvation model based on SCRF calculation. It is a simpler model of solution than the continuous solvation model and only considers the solvent as a continuous dielectric with a cavity accurately modeled for the solute.

The molecular interaction energies of complexes in water ΔE_{AB} are calculated by the supermolecular method [31] as follows:

$$\Delta E_{AB} = E_{AB} - E_A - E_B \quad (10)$$

Here AB, A, and B are the inclusion complexes of α -CD + nitriles, α -CD, and aliphatic nitriles in water, respectively. The calculated results are listed in Table 5. As shown in Table 5, stabilizations of conformers of

Table 5 Interaction energies (ΔE_{AB} /Hartree) by Eq. 9 of the minimum energy forms of aliphatic nitriles 1:1 α -cyclodextrin compounds calculated by DFT B3LYP/6-31G** in SCRF

Guest	ΔE_{AB} /Hartree		
	Inclusion compound	In gas phase	In aqueous solution
EtCN	α CD-EtCN	-0.009925	-0.002002
PrCN	α CD-PrCN	-0.004137	-0.001158
BtCN	α CD-BtCN	-0.008121	-0.005041
PeCN	α CD-PeCN	-0.002952	-0.003042
	3C-PeCN	-0.01162	-0.10666
HxCN	α CD-HxCN	-0.002025	-0.0035626
	5G6C-HxCN*	-0.01061	-0.020540
HpCN	α CD-HpCN	-0.002288	-0.0008175
	5C6G7C-HpCN*	-0.017771	-0.008474
OtCN	α CD-OtCN	-0.0007400	-0.001934
	4C5G6C-OtCN*	-0.011163	-0.005751

Two conformers of aliphatic nitriles from pentanenitrile to butanenitrile were calculated

Without asterisk marks were all *trans* conformation. With asterisk mark were the shortest distance conformer between head and tail of nitriles. C cis conformer; G gauche conformer

guest + α -CD were different in the gas phase and in aqueous solution. The *trans* conformers were less stable than other conformers for pentane nitrile to octane nitrile.

Also the stabilities of guest molecules in the α -CD cavity by means of Gaussian calculation were reported for pentane derivatives [12]. The insert direction of guest molecules to the α -CD cavity was not the same for pentane derivatives. And the guest molecule of pentane nitrile was inserted from the second hydroxyl groups of α -CD. Other aliphatic nitriles have a similar mechanism for inclusion. So non-polar interactions between α -CD and aliphatic nitriles in water were calculated by the difference between B97D/6-311++G** and B971/6-311++G** [34, 35], which were calculated with non-polar interaction and without non-polar interaction, respectively. The results are listed in Table 6. The geometry of the complexes completely optimized any restriction in water solution by using the Onsager continuum solvation model based on SCRF calculation.

As shown in Tables 6 and 7, major interaction energies by the inclusion of guest molecules in the α -CD cavity might be non-polar interactions between the α -CD cavity and non-polar parts of aliphatic nitriles. And bulky conformation of aliphatic nitriles might help to increase the stabilization of non-polar interactions between α -CD and aliphatic nitriles.

The correlation between the inclusion enthalpies observed and interaction energies is shown in Fig. 5. There is a loose correlation except for in the pentane nitrile

Table 6 Interaction energies ΔE_{AB} with nonpolar, without nonpolar and difference between those of non-polar and polar of aliphatic nitriles 1:1 α -cyclodextrin compounds in kJ mol^{-1}

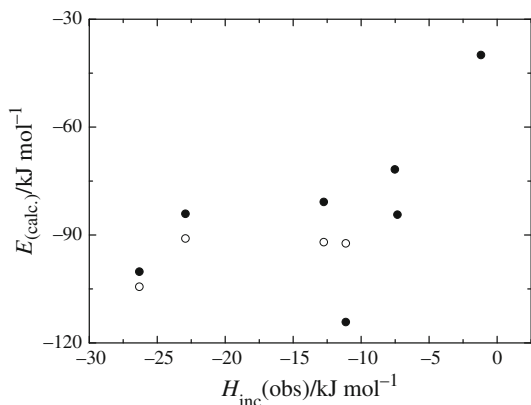
Inclusion compound	E_{WNP}	E_{WONP}	ΔE
α CD-EtCN	-37.40	-2.54	-39.95
α CD-PrCN	-60.83	-10.92	-71.75
α CD-BtCN	-79.69	-1.65	-84.35
α CD-PeCN	-118.5	-58.72	-114.2
α CD-3C-PeCN	-86.01	-6.32	-92.33
α CD-HxCN	-114.3	-30.16	-84.10
α CD-5G6C-HxCN*	-77.95	-13.04	-90.99
α CD-HpCN	-90.52	-9.66	-100.2
α CD-5C6G7C-HpCN*	-138.0	-33.59	-104.4
α CD-OtCN	-120.6	-39.75	-80.81
α CD-4C5G6C-OtCN*	-131.7	-39.75	-91.99

E_{WNP} and E_{WONP} were calculated by B97D/6-31G*, E (B971/6-31G*) in SCRF, which were interaction energies with nonpolar, without nonpolar interactions. ΔE were difference between E_{WNP} and E_{WONP} . Without asterisk marks were all *trans* conformation. With asterisk mark were the shortest distance conformer between head and tail of nitriles. C cis conformer, G gauche conformer

Table 7 Best fit coefficients of Eq. 10

System	a	b	$s_f/\text{kJ mol}^{-1}$
Nitril + alc+	0.921	3.7	23.5
Nitrile	24.2	0.894	3.4
Alcohol	22.3	0.911	4.4

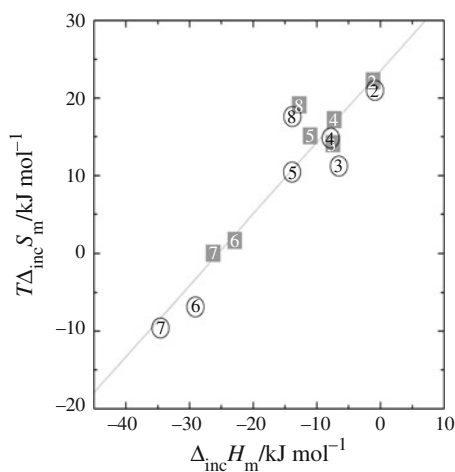
$$T\Delta S/\text{kJ mol}^{-1} = a + b \times \Delta H$$

**Fig. 5** Correlation between inclusion enthalpies observed and interaction energies: *filled circle* all *trans* conformer, *open circle* the bulkiest conformers form pentane nitrile to octane nitrile

system. And the appearance might be different on the boundary of the pentane nitrile system.

Entropy and enthalpy compensation

Correlations between the entropy and enthalpy of inclusion of aliphatic nitriles are shown in Fig. 6 with aliphatic

**Fig. 6** Correlation between enthalpies and entropies of inclusion: *filled square* R-CN, *open circle* R-OH cited from [7]; figures show the number of the methylene group

alcohols from methanol to octanol, which have been reported [7, 12] previously. There is a linear relation as shown in Fig. 6 following Eq. 11.

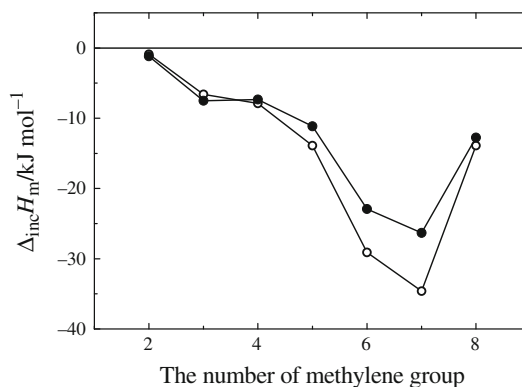
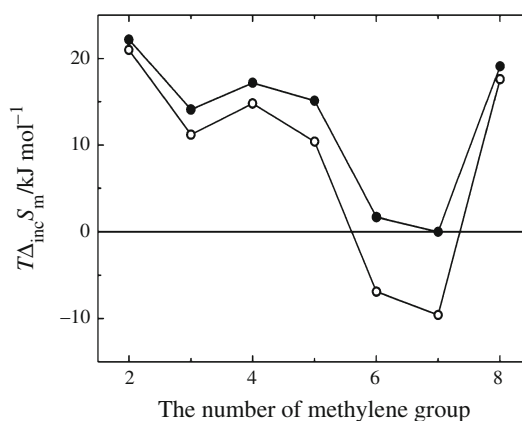
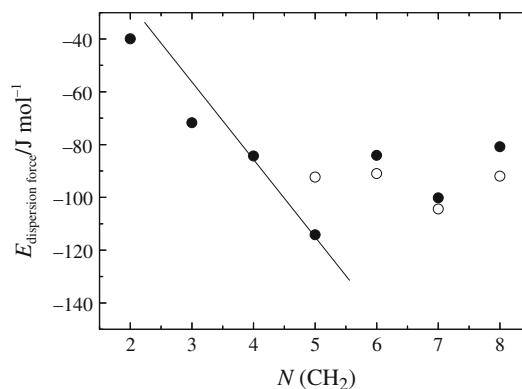
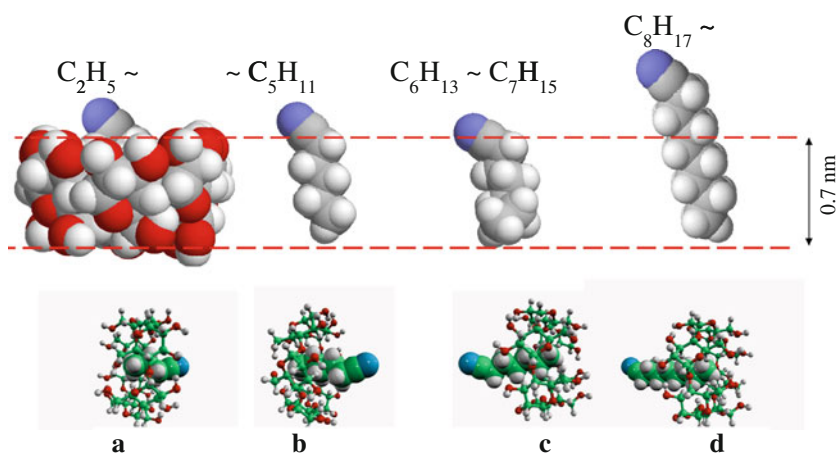
**Fig. 7** The change of enthalpies of inclusion α -CD + guest molecules at 298.15 K against the number of alkyl chains: *filled circle* aliphatic nitriles, *open circle* aliphatic alcohols**Fig. 8** The change of entropies of inclusion α -CD + guest molecules at 298.15 K against the number of alkyl chains: *filled circle* aliphatic nitriles, *open circle* aliphatic alcohols**Fig. 9** Energies of inclusion for different conformers for 1-H(CH₂)_n CN: $n = 1-8$: *filled circle* all *trans* conformer, *open circle* the bulkiest conformers form pentane nitrile to octane nitrile

Fig. 10 Inclusion position of aliphatic nitriles + α CD in water by Gaussian results: **a**, propane nitrile + α CD; **b**, pentane nitrile + α CD; **c**, hexane nitrile + α CD; **d**, octane nitrile + α CD



$$T\Delta S/\text{kJ mol}^{-1} = 23.5 + 0.921\Delta H, \quad s_f = 3.7 \text{ kJ mol}^{-1} \quad (11)$$

However, the relations of aliphatic nitriles were slightly upside from Eq. 11 and aliphatic alcohols were slightly downside. And the relations of octanol and octane nitrile were upside from Eq. 11. When the aliphatic chain was increased, the enthalpies of inclusion become more stable and entropies of inclusion were less stable except the system of butane nitrile; however, the system of octane nitrile and octanol showed different behavior to the others in both groups. The results suggest that the size effect of aliphatic groups on inclusion on stability, that is the hydrophobic interaction between the α -CD cavity and guest molecules, was less effective than the polar groups of hydroxyl and nitrile in guest molecules.

Number of methylene groups' effect of aliphatic nitriles on inclusion

The correlation between enthalpies and entropies of inclusion of aliphatic nitriles + α -CD and the number of methylene groups are shown in Figs. 7 and 8, respectively. Also the correlation of α -CD + aliphatic alcohols [7, 10, 11] is also shown in those figures. The thermodynamic properties of inclusion for both systems are similar. Enthalpic stabilization of inclusion was increased with increasing the size of aliphatic groups except octane nitrile and octane-1-ol. Those increasing ratios of stabilization on inclusion with the number of methylene groups were not constant. There are slight differences in behaviors between aliphatic nitriles of odd and even numbers of aliphatic groups as well as the previously reported system of aliphatic alcohols. The results might show that the inside wall of α -CD can recognize odd and even numbers of aliphatic groups. There is some correlation between the physical properties of organic complexes and the number of methylene groups, the so-called odd–even rule [36–38]. To

confirm major interactions for these phenomena, non-polar interaction energies between α -CD and aliphatic nitriles are shown in Fig. 10. Non-polar interaction that is dispersion force was calculated by DFT B97D/6-311++G** and B971/6-311++G** [34, 35]. Non-polar interaction was increased with increasing the number of methylene groups in aliphatic nitriles from ethane nitrile to pentane nitrile, but all *trans* conformers that form pentane nitrile to octane nitrile showed an odd–even difference as shown in Fig. 9. It may not be denied that it is some odd–even difference for the bulkiest conformers form pentane nitrile to octane nitrile.

Configurations of aliphatic nitriles in the inclusion complex of α -CD in aqueous solution by quantum chemical calculation are shown in Fig. 10. As shown in Fig. 10, the depth of the α -CD cavity is about 0.7 nm [29]. The lengths of aliphatic nitriles were increased with increasing the number of methylene groups in aliphatic nitriles. Some methylene groups in aliphatic nitriles did not completely enter the α -CD cavity and emerged outside the α -CD cavity. The hydrophobic part of aliphatic nitrile might change inclusion environments not only in the α -CD cavity but also the hydration of water.

Conclusions

The enthalpies and entropies of inclusion of α -CD with seven aliphatic nitriles were determined. The enthalpies of inclusion were increased with increasing the non-polar parts of aliphatic nitriles, but entropies of inclusion were decreased with increasing the non-polar parts of aliphatic nitriles, except octane nitrile. The Gibbs energies of inclusion of α -CD with seven aliphatic nitriles were larger than -23 kJ mol^{-1} . The forces of inclusion for α -CD with aliphatic nitriles were driven by the two major factors of entropy and enthalpy. Non-polar interactions between α -CD and aliphatic nitrile were calculated and showed a

major effect for inclusion of aliphatic nitriles in the α -CD cavity.

Entropy–enthalpy compensation correlation was shown for the inclusion complexes of α -CD + aliphatic nitriles. The slope of α -CD + aliphatic nitriles and + aliphatic alcohols were similar but the latter system was slightly larger than the former system.

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